

## CASE REPORT

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# Surgical Treatment of Pancreatic Metastases of Renal Cell Carcinoma

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### ABSTRACT

**Context** The pancreas is an unusual site for metastases of renal cell carcinoma origin, sometimes occurring many years after nephrectomy. We herein present two cases of pancreatic metastases of renal cell carcinoma which occurred 17 and 19 years after the primary diagnosis.

**Case report** In the first case, metastases were found in the head of the pancreas, upper right arm and the right lobe of the thyroid gland. In the second case, a tumor was found in the tail of the pancreas and a remnant of the right kidney. This was the third recurrence of the original tumor after an initial left nephrectomy and two subsequent partial right nephrectomies in the past. Treatment in the first case consisted of excision of the tumor in the upper right arm, a Whipple operation, and a thyroidectomy. In the second case, a distal pancreatectomy and remnant right nephrectomy were undertaken. Both patients recovered from the operations without complications and remain free of tumor in follow-up periods of 54 and 8 months respectively.

**Conclusions** Resection of renal cell carcinoma metastases involving the pancreas provides satisfactory long-term survival, and should be undertaken whenever possible.

### INTRODUCTION

Renal cell carcinoma (RCC) is a malignant tumor of unique biological behavior, presenting, in some cases, with very late metastases. The pancreas is an unusual site for such metastases. In such cases, the differential diagnosis includes mainly primary pancreatic tumors, and the diagnosis of metastatic RCC is frequently made at the time of microscopic examination.

In this study, we present two cases of late pancreatic metastases of RCC which occurred 17 and 19 years after the diagnosis of the primary tumor; they were successfully treated surgically.

### CASE REPORT

#### Case 1

A 70-year-old man presented in January 2000 with acute gastrointestinal bleeding. His past medical history showed that he had undergone a left nephrectomy in 1983 for renal cell carcinoma (pT2 pN0 Mx, G2). Endoscopy revealed a tumor in the head of the pancreas extending into the duodenum. Based on quick contrast mean absorption in computed tomography-scan images (Figure 1) and positivity for chromogranin A (676 µg/L; reference range: 0-100 µg/L) in laboratory testing, the tumor was suspected to be of neuroendocrine origin. CEA, CA 19-9, CA

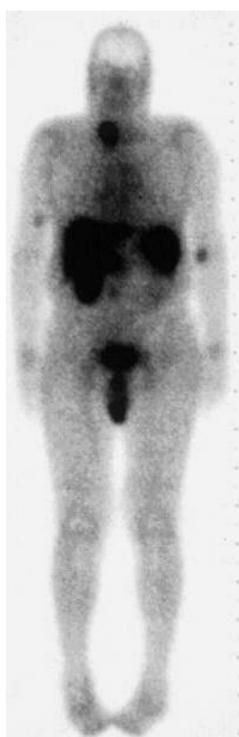


**Figure 1.** A computed tomography scan of the abdomen showing the tumor in the head of the pancreas. Quick contrast mean absorption was incorrectly interpreted as indicative of a tumor of neuroendocrine origin.

15-3, 5-hydroxyindoleacetic acid and serotonin were within normal laboratory range values. Further physical examination showed a movable 2x3x3 cm tumor in the soft tissues of the upper right arm. Somatostatin receptor scintigraphy showed a pathological uptake in the head of the pancreas, upper right arm, and right lobe of the thyroid gland (Figure 2). Thyroid gland scintigraphy showed a cold node in the base of the right lobe. Given the

localized nature of the lesions, and the absence of further suspicious masses, it was decided to proceed with surgical resection.

Excision in toto of the tumor in the upper right arm revealed metastatic renal cell carcinoma. A Whipple operation with resection and reconstruction of the portal vein was performed two weeks



**Figure 2.** Somatostatin receptor scintigraphy showing a pathological uptake in the head of the pancreas, the upper right arm, and the right side of the thyroid gland.

later (Figure 3), aimed at preventing further upper gastrointestinal hemorrhage. The postoperative course was uneventful. Histological exam showed pancreatic metastases of renal cell carcinoma, with tumor-free resection margins. Six weeks later, a total thyroidectomy was performed based on the macroscopic intraoperative suspicion of multifocal metastases in both lobes of the thyroid glands. Histopathological evaluation of the resected specimen demonstrated RCC metastatic disease in the right thyroid lobe. Immunohistochemistry was negative for chromogranin A in all cases. Nevertheless, chromogranin A levels returned to 152 µg/L after the resections.

Fifty-four months after surgical treatment, the patient is in excellent health with no evidence of residual or new tumor growth as evidenced by imaging, biochemical and clinical follow-up exams.

## Case 2

In 1985, a 54-year-old woman underwent a left nephrectomy for renal cell carcinoma (pT1 N0 M0) at another hospital. Because of a new RCC lesion in the right kidney (also pT1 N0 M0), the patient had a partial right nephrectomy in 1993. In November 2002, the patient underwent a second kidney-preserving



**Figure 3.** Surgical specimen of the Whipple operation demonstrating a 5.5x6x5 cm tumor in the head of the pancreas.



**Figure 4.** Surgical specimen of the distal pancreatectomy.

partial right nephrectomy for recurrent RCC at another institution. In February 2004, the patient presented at our hospital with a mass in the right kidney remnant and a 2.7 cm lesion in the tail of the pancreas. Informed consent addressing the risks of the surgery was obtained, with special emphasis on the need for lifelong hemodialysis. A remnant right nephrectomy and distal pancreatectomy without splenectomy were performed (Figure 4). A Cimino-shunt was constructed in the left forearm two weeks later. The patient remains recurrence-free 8 months postoperatively.

## DISCUSSION

The pancreas is an unusual but occasionally favored site for metastases, notably from carcinomas of the kidney and lung. In a clinical series of patients with pancreatic tumors, 4.5 % of cases were found to be metastatic lesions. That figure increased to 42% among patients with previously diagnosed malignancies and solitary lesions in the pancreas [1]. Pancreatic metastases of RCC origin represented between 0.25 and 3% of all resected pancreatic specimens in a recent large series [2, 3]. Among patients who had resections of RCC and survived for 10 years, more than 10% had late metastases [4]. The median interval from nephrectomy to diagnosis of solitary pancreatic metastases was reported to be 11 years [5]. Cases of a long-term disease-free interval between a nephrectomy and pancreatic metastases have

been reported, the longest one being 28 years [6, 7, 8].

The mode of spread of RCC to the pancreas remains controversial. It may be hematogenous, along the draining collateral veins from a hypervascular primary tumor, or lymphatic by retrograde flow through retroperitoneal nodes [9].

The current literature contains no data supporting medical treatment of patients with isolated RCC metastases, even though there is some evidence that patients who do not undergo resection still have a reasonable long survival rate [3, 10]. Spontaneous regression of pancreatic metastasis of RCC has also been reported [11]. The effectiveness of adjuvant therapy with alpha-interferon for RCC metastases in the pancreas has not yet been proven [10, 12].

Some authors consider pancreatectomy for metastatic disease as long as the pancreas is the only site of metastasis [1]. However, the slow metastatic pattern of RCCs could justify pancreatic resections even in cases where another metastatic lesion is simultaneously identified. In a retrospective analysis of 151 patients with metastatic RCC involving, for the most part, the lungs, bone and lymph nodes, but not the pancreas, 111 patients with multifocal metastases and 40 patients with solitary metastases underwent surgical resection. No survival benefit was observed for those with solitary metastases, but survival was found to be significantly higher after a R0 resection, independent of the number of tumor lesions [13]. Kavolius *et al.*, in a retrospective study of 278 cases of metastatic RCC (mostly in the lungs and the brain), showed a 5-year survival rate of 44% after R0 resections as opposed to 14% after palliative or incomplete resections. Five-year survival was also better for patients with solitary as opposed to multifocal metastases (54% vs. 29%, respectively) [14].

Cases of both synchronous and asynchronous bilateral RCC with late pancreatic metastases have been observed in the past. Carini *et al.* reported a case of solitary pancreatic metastases 13 years after a left radical nephrectomy and right lower polar resection

for bilateral simultaneous RCC, successfully treated with a pancreaticoduodenectomy [15]. Gohji *et al.* reported a case of asynchronous bilateral renal cell carcinoma with pancreatic metastasis treated with distal pancreatectomy more than 6 and 2 years after a left nephrectomy and right renal tumor enucleation, respectively. The patient was alive without disease after being treated with alpha-interferon for 12 months after distal pancreatectomy [12].

Solitary pancreatic metastases are considered to be more frequent than multifocal ones [2]. Standard pancreatic resections are adopted in the surgical therapy of pancreatic metastases of RCC: pancreaticoduodenectomy for tumors in the head, neck or uncinate process, distal pancreatectomy with or without splenectomy for tumors in the body or tail, total pancreatectomy for multifocal lesions, or atypical tumor resection in other cases. Bassi *et al.*, based on a morbidity rate of 83% and a recurrence rate of 50% after atypical resections, recommended standard pancreatic resections in cases of RCC metastases [16]. Given that many studies report no pancreatic lymph node involvement in the surgical specimens [3, 17], radical lymph node dissection does not seem to be mandatory [3]. Kierney *et al.* reported a 5-year survival rate of 31% in 41 cases of intrathoracic, intracranial, intraabdominal, or extrapleural chest wall soft tissue metastatic RCC undergoing resection. Single lesions were found in 64% of the cases, and complete tumor removal was achieved in 88% of cases [18]. A 5-year survival rate of approximately 70% has been noted in some recent reports [6, 19]. Thompson and Heffess reported a series of 21 patients who underwent pancreatic resection for RCC metastases with an 81% 5-year survival rate. Mean overall survival from the date of nephrectomy was 19.8 years, and mean overall survival from the date of diagnosis of pancreatic metastasis was 6.2 years [2].

An obvious limitation of our report is the short follow-up, especially in the second case. However, as mentioned above, long term survival after surgical therapy of pancreatic

metastases of RCC is well-documented in the literature [2, 6, 19].

Surgical therapy in both of our cases could be characterized as extreme. In the first case, tumor infiltration of the portal vein required a technically demanding pancreaticoduodenectomy with partial resection and reconstruction of the portal vein. Metastases in the upper right arm and in the thyroid gland were also addressed surgically. Similar aggressive surgical therapy was reported in the series of Law *et al.*, where 3 patients underwent resection of brain, lung, and adrenal gland metastases from RCC prior to pancreatic resection [20]. In our second case, a remnant nephrectomy led to renal insufficiency requiring lifelong hemodialysis. However, the strong desire of the patients to achieve 'tumor-free' situations together with the encouraging reports in the literature encouraged us to proceed with the above-mentioned therapies.

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**Keywords** Carcinoma, Renal Cell; Neoplasm Metastasis; Pancreatectomy; Pancreatic Diseases

**Abbreviations** RCC: renal cell carcinoma

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